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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/644,703	08/19/2003	Louis A. Pena	30817-1008-CIP	7990

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EXAMINER	
DANG, IAN D	

ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/644,703	PENA ET AL.	
	Examiner	Art Unit	
	Ian Dang	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-59* is/are pending in the application.

4a) Of the above claim(s) *1-7,21-26 and 46-59* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-20 and 27-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-59* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08/19/2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/22/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to the amendment and response filed on 04/17/2007. Claims 1-7, 21-26, 46-59 have been withdrawn. Claims 8-20 and 27-45 are pending and under examination.

Priority

At page 13 of the response, Applicant alleges that the '268 application provides numerous teachings and examples that provide adequate support or enablement in the manner provided for by First paragraph 35 U.S.C. 112 for one or more claims of the present application.

Applicant's arguments have been fully considered but are not found persuasive. As disclosed in the previous Office action mailed 10/17/2006, the claimed invention drawn to a heparin-binding growth factor (HBGF) analog of formula II. The heparin-binding growth factor (HBGF) analog of formula II in the U.S. application 10/224,268 has a different formula II from the one disclosed in the instant application: U.S. application 10/644,703 filed on 08/19/2003. Therefore, the instant application is given the priority of the U.S. application 10/644,268 filing date of 08/19/2003.

Rejections Withdrawn

Double Patenting

Applicant's response and arguments filed on 04/17/2007 have overcome the rejection of claims 8-20 and 27-45 under Double Patenting (see page 13 of the response filed 04/17/2007). The rejection of claims 8-20 and 27-45 under Double Patenting has been withdrawn.

Rejections Maintained

Claim Rejections - 35 USC § 112 (Written Description)

Claims 8-20 and 27-45 are rejected under 35 U.S.C. 112 First paragraph as failing to comply wit the written description requirement. The basis for this rejection is set forth for claims 1-8 and 27-45 at page 4 of the previous Office action of 17 October 2006.

The rejection of claims 8-20 and 27-45 is maintained. Applicant's response and arguments filed on 04/17/2007 have been fully considered but they are not persuasive.

(i) At page 14 of the response, Applicant argues that the specification clearly states that the members of the genus all share the feature of binding selectively to heparin and all share the feature of incorporating a growth factor sequence that binds to a growth factor receptor with examples of growth factors provided at line 9, page 11-lines 10, page 12, or an analogue thereof. In addition, Applicant argues that all members of the genus share the features of A) peptide chains that binds a heparin-binding growth factor receptor, B) a hydrophobic linker, and C) a heparin-binding domain.

Applicant's arguments have been fully considered but are not found persuasive. To provide adequate written description and evidence of possession of claimed genus, the specification must provide efficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure/function correlation, and other identifying characteristics. Accordingly, in the absence of sufficient recitation of distinguishing structural/physical and identifying characteristics, the specification does not provide adequate written description of the claimed genus.

The guidance indicated by Applicant in the specification of the instant application does not satisfy the written description requirement because the specification recites general characteristics regarding the heparin-binding growth factor analog of formula II without any sufficient recitation of distinguishing structural/physical and identifying characteristics of the polypeptide. In claim 8 Applicant does not recite any specific or structural features of the HBGF analog of formula II. For instance, the claim recites that each X is a peptide chain that (i) has a minimum of three amino acid residues, (ii) has a maximum of about fifty amino acid residues, and (iii) binds a heparin-binding growth factor receptor (HBGFR), but it does not disclose any identifying characteristics of each component X, Y, and Z with the biological activity of the HBGF analog of formula II.

While the specification discloses the general characteristics of the HBGF analog (page 11, lines 9 to page 12 line 12)), Applicant has not provided any specific identifying structural characteristics to that one skill level in art can correlate with a distinct biological function. At page 11 of the specification, Applicant discloses that HBGFs include any growth factor that binds selectively to heparin (line 9) and recites a long list of growth factors (pages 11 and 12), but does not provide any structural distinguishing characteristics from any of these growth factors. Applicant has provided the biological activity of binding to heparin, but Applicant has not provided any correlation between the biological activity of the HBGF analog and its identifying structural feature.

In addition, the abstract does not provide sufficient teachings correlating the structure of the HBGF analog with its biological function. Specifically, although in the abstract of the application Applicant has provided characteristics for the genus that share features of A) peptide chains that binds a heparin binding growth factor B) a hydrophobic linker, and C) a heparin binding domain, these teachings provide general disclosure regarding the HBGF analog but do

not provide any specific characteristics, so that one skill in the art can identify the claimed HBGF analog of the instant application.

(ii) At page 14 of the response, Applicant states that in the specification (lines 20-27) that the analogue binds to its cognate partner growth factor receptor or a different growth factor receptor. Thus the limitation is set as receptor binding. Those skilled in the art would appreciate that given receptor binding as the central limitation, then amino acid substitutions, deletions, insertions, and/or additions could be used to modify the nature of the receptor binding. In addition, Applicant argues that the peptides of this invention are limited in the invention to polypeptides containing three specific components: A) peptide chains that bind a heparin-binding growth factor receptor, B) a hydrophobic linker, and C) a heparin-binding domain. Further the specification as originally filed includes a teaching of homologous sequences and percent homology preferred. In addition, there is a strong presumption that an adequate written description of the claimed invention is present when the application is filed.

Applicant's arguments have been fully considered but are not found persuasive. As discussed above, the function of the analogue of binding to a receptor is not sufficient to meet the written description requirement because Applicant has not provided any identifying structural characteristics correlating with that function. As disclosed previously, Applicant has not satisfied the disclosure of complete or partial structure/function correlation, and other identifying characteristics. In addition, Applicant indicates that HBGF analog comprising conservative substitutions, insertions, or deletions that retain the biological activity of receptor that are within the scope of the invention. However, Applicant only provides a general disclosure regarding the HBGF analog and does not provide any specific characteristics, so that one skill in the art can identify the claimed polypeptide of the instant application. Additionally, the broad brush

discussion of making and screening for analogs does not constitute a disclosure of a representative number of members (page 15, lines 10-25). No such analogs were made or shown to have activity. The specification's general discussion of making and screening for analogs constitutes an invitation to experiment by trial and error. Such does not constitute an adequate written description for the claimed HBGF analogs.

Moreover, the 3 structural components of the polypeptides are not sufficient to meet the written description requirement as disclosed above. Specifically, although in the abstract of the application Applicant has provided characteristics for the genus that share features of A) peptide chains that binds a heparin binding growth factor B) a hydrophobic linker, and C) a heparin binding domain, these teachings provide general disclosure regarding the HBGF analog but do not provide any specific characteristics, so that one skill in the art can identify the claimed HBGF analog of the instant application.

Claim Rejections - 35 USC § 112 (Enablement)

Claims 8-20 and 27-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the synthetic HBGF analog of Formula II (species F2A4), does not reasonably provide enablement for variants of the synthetic HBGF analog. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims. The basis for this rejection is set forth for claims 8-20 and 27-45 of the previous Office action of 17 October 2006.

The rejection of claims 8-20 and 27-45 is maintained. Applicant's response, arguments, and amendments of claims 8-20 and 27-45 have been fully considered but they are not persuasive.

(i) Applicant argues that it would be obvious to those skilled in the art to identify additional receptor binding sequences, which would be incorporated into the current invention. It would further be obvious to those skilled in the art that a "cassette approach could be used to produce other compounds of Formula II by keeping constant the given a heparin-binding domain and hydrophobic linker and rotating the peptide chains that binds a heparin-binding growth factor to change receptor specificity.

Applicant's arguments have been fully considered but are not found persuasive. While Applicant discloses that it would be obvious to produce other compounds of Formula II, the specification does not disclose how to make/use the claimed HBGF analog. The specification of the instant application only provides general characteristics regarding the structure of HBGF analog without providing any distinguishing characteristics for any of the analogs.

Although Applicants have disclosed that the HBGF analog binds to one or more of the receptors bound by the particular HBGF (page 11, line 5) with a functional limitation with respect to the analog, Applicants have not provided sufficient disclosure regarding the identifying and structural characteristics of the analog. The specification does not provide any guidance regarding the identifying structural characteristics with respect to the each component of the analog. For instance, the specification discloses of A) peptide chains that binds a heparin binding growth factor B) a hydrophobic linker, and C) a heparin binding domain. These general teachings encompasses a large number of possible peptides binding to the heparin receptor. However, the specification does not provide any guidance for any identifying characteristics needed for each component of the peptide required for the peptide to bind to heparin. Without sufficient disclosure in the specification, it would require undue experimentation for one of skill in the art to be able to make/use the HBGF analog.

(ii) At page 16 of the response, Applicant presents the governing law and USPTO patent examining procedure on enablement and point by point rebuttal of Examiner's asserted Wands' factors analysis.

Breath of the claims

Applicant argues that detailed teachings as to the criteria for producing other compounds of formula II, which are discussed in the Written Description rejection above. In addition, Applicant wishes to point out that the independent claims do not recite that the activity of the Formula II compounds have an activity to the full force and effect as that of F2A4.

Applicant's arguments have been fully considered but are not found persuasive. As described above, the recitation of claim 8 encompasses a large number of HBGF. For instance, the specification recites that the structural feature for the HBGF analog includes any growth factor that binds to heparin and discloses a long list of growth factors (pages 11-12). In addition, while the independent claim does not recite the Formula II compounds having the activity of F2A4, the F2A4 is a working example for the HBGF analog of formula II and should have the activities of other HBGF analog of formula II.

Unpredictability in the art

At page 22 of the response, Applicant argues that the X portion of the analogue binds to a heparin binding growth factor (HBGF) receptor and/or has homology as defined on page 14 lines 1-9 to the cognate peptide for the receptor as described on page 14 lines (20-27) of the specification. With respect to the critical features of the invention, the amino acid sequence is actually highly predictable. In addition, Applicant cites In re Vaek to support enablement for the claimed invention.

Applicant's arguments have been fully considered but are not found persuasive. Although Applicant discloses the functional limitation for the HBGF analog, the specification does not disclose any distinguishing structural characteristics for the components of the peptide that can predictably result in the binding of the receptor. As recited on page 7 in the previous Office actions mailed 10/17/2006, several references teach that manipulations and mutations of heparin- binding domains of growth factors (Yoneda, et al, 2000, Nature Biotech, 18: 641-644; Verrecchio, et al, 2000, J. Biol. Chem., 275(11): 7701-7707) result in functionally-different compounds. These examples and others illustrate that it is not predictable as to which amino acids and analogs are necessary to maintain the functional characteristics of a synthetic peptide analog. Without sufficient disclosure in the specification, it would require undue experimentation for one of skill in the art to be able to make/use all possible HBGF analogs encompassed by the claims.

The quantity of experimentation necessary

At page 24 of the response, Applicant points out the standard of enablement with respect to undue experimentation and the quantity of experimentation set forth in the MPEP. In addition, Applicants whish to point out that making the peptides recited in the present claims was, as disclosed in the originally filed specification as discussed hereinabove, a routine matter achievable by conventional peptide synthesis technology as of the filing date and earliest priority date of the present application as discussed above.

Applicant's arguments have been fully considered but are not found persuasive. Although the Examiner acknowledges that the method of synthesizing peptides is routine in the art, undue experimentation is required with respect to the HBGF analogs themselves. The specification of the instant application only provides general characteristics regarding the

structure of HBGF analog without providing any distinguishing structural characteristics for any of its analogs. The specification does not provide any guidance regarding the identifying structural characteristics with respect to each component of the analog required for binding heparin. Thus one of skill in the art would know how to make the HBGF analog from the teachings provided by Applicant in the specification. Without sufficient disclosure in the specification, it would require undue experimentation for one of skill in the art to be able to make and use the HBGF analog claim in the instant application.

Claim Rejections - 35 USC § 112 (Second paragraph)

Claims 8-20 and 27-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The basis of the rejection is set forth for claims 8-20 and 27-45 of the previous Office action of 17 October 2006.

The rejection of claims 8-20 and 27-45 is maintained. Applicant has not responded to the rejection in the response filed on 04/17/2007.

Claims 8-20 and 27-45 are rejected as being indefinite because claims 8 and 11 recite an HBGF chain comprising a number of "atoms." However, one skilled in the art cannot determine the metes and bounds of the claimed invention because one does not normally count the atoms (e.g., C, H, O, N) in a polypeptide chain, but rather amino acids. Amending claims to recite "amino acids" or "residues," for example would be remedial.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ian Dang whose telephone number is (571) 272-5014. The examiner can normally be reached on Monday-Friday from 9am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ian Dang
Patent Examiner
Art Unit 1647
June 23, 2007

Bridget E. Bunner

BRIDGET BUNNER
PATENT EXAMINER